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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/492,028	01/26/2000	Charles S. Zuker	02307E- 092610	9361

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EXAMINER

BUNNER, BRIDGET E

ART UNIT PAPER NUMBER

1647

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/492,028

Applicant(s)

ZUKER, CHARLES S.

Examiner

Bridget E. Bunner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 5 and 9-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 6-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-24 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Continued Prosecution Application

The Request for Continued Examination (RCE) filed on 14 November 2002 (Paper No. 24) under 37 CFR 1.114 based on parent Application No. 09/492, 028 is acceptable and an RCE has been established. An action on the RCE follows.

Status of Application, Amendments and/or Claims

The amendment of 14 November 2002 (Paper No. 25) has been entered in full. Claims 1 and 6 are amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4 and 6-8 are under consideration in the instant application.

Election/Restrictions

It is noted to Applicant that this application contains *pending* claims 5 and 9-24 drawn to an invention nonelected without traverse in Paper No. 10 (22 December 2000). In the Office Action of 11 February 2002 (Paper No. 16), the Examiner indicated that a complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Therefore, claims 5 and 9-24 remain withdrawn from further consideration.

Withdrawn Objections and/or Rejections

1. The rejection of claims 1-4 and 6-8 under 35 U.S.C. § 112, second paragraph at pg 3-4 of the previous Office Action (Paper No. 16, 11 February 2002) and at pg 5 of the Office Action of

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07 February 2001 (Paper No. 11) is *withdrawn* in view of the amended claims and Applicant's persuasive arguments (Paper No. 25, 14 November 2002).

2. The rejection of claims 1-4 and 6-8 under 35 U.S.C. § 103(a) at pg 4-5 of the previous Office Action (Paper No. 16, 11 February 2002) and at pg 6-7 of the Office Action of 07 February 2001 (Paper No. 11) is *withdrawn* in view of the amended claims and Applicant's persuasive arguments (Paper No. 25, 14 November 2002).

Specification

3. The objection to the specification regarding the issue of patent applications being referenced throughout the disclosure is maintained and held in abeyance until allowable subject matter is identified. Although Applicant has updated the status of U.S. Application No. 09/361,631 in numerous sections of the instant specification, U.S. Application No. 09/361,652 remains pending. This objection will be maintained until the referenced application (09/361,652) is abandoned or allowed or if the instant application is deemed allowable.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-4 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, claims 1-4 and 6-8 are directed to a method for identifying a compound that modulates signal transduction in taste cells, comprising the steps of (i) contacting a cell which expresses a taste cell specific G-protein alpha subunit polypeptide and a taste cell specific G protein coupled receptor with the compound, the G-protein alpha subunit polypeptide comprising greater than 70% amino acid sequence identity to a polypeptide having a sequence of SEQ ID NO: 2; and (ii) determining a functional effect of the compound upon the cell expressing the taste cell specific G-protein alpha subunit polypeptide and the taste cell specific G protein coupled receptor, thereby identifying a compound that modulates signal transduction in taste cells. The claims also recite that the functional effect is determined by measuring increased or decreased binding of radiolabeled GTP to the G-protein alpha subunit polypeptide or to a G protein comprising the G-protein alpha subunit polypeptide. The claims recite that the that G-protein alpha subunit polypeptide comprises an amino acid sequence of SEQ ID NO: 2 and is expressed in a cell or a cell membrane.

The specification teaches that G α 14, a G-protein alpha subunit, is specifically and selectively expressed in taste receptor cells and is co-expressed with G-protein coupled taste receptors, GPCR-B3 and GPCR-B4 (pg 4, lines 3-6). The specification also discloses that the G α 14 protein can be isolated, expressed in a cell, expressed in a membrane derived from a cell, or expressed in tissue or in an animal. The specification indicates that tongue slices, dissociated cells from a tongue, transformed cell, cell membranes, or lipid bilayers can be utilized (pg 26, lines 15-18). The specification discloses that any suitable physiological change that affects TC-G α 14 activity can be used to assess the influence of a test compound on the polypeptides of the invention (pg 26, lines 24-27). However, the specification does not teach contacting any cell

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which expresses a taste cell specific G-protein alpha subunit polypeptide (with 70% amino acid sequence identity to SEQ ID NO: 2) and any taste cell specific G-protein coupled receptor with any compound and determining the functional effect of the compound upon the cell to identify a compound that modulates signal transduction in taste cells. According to MPEP § 2164.06, “the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed. For example, if a very difficult and time consuming assay is needed to identify a compound within the scope of the claim, then this great quantity of experimentation should be considered in the overall analysis”.

The specification of the instant application does not disclose the identity of any substance capable of modulating signal transduction in taste cells via the claimed method. The prophetic procedure for screening a compound that modulates signal transduction in taste cells is not adequate guidance, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Furthermore, since the specification provides no guidance regarding what sort of compounds should be screened for the desired activity, the skilled artisan must resort to trial and error experimentation to determine which class of compounds might yield one with the desired activity. Such trial and error experimentation is considered undue. Therefore, undue experimentation would be required of the skilled artisan to contact a cell which expresses numerous possible variants of a G-protein alpha subunit polypeptide of SEQ ID NO: 2 and any taste cell specific G protein coupled receptor with any type of compound. There is also little guidance in the specification or the claims indicating which taste cell specific G protein coupled receptor is expressed or whether the G-protein alpha

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subunit polypeptide and the taste cell specific G protein coupled receptor are endogenous to the taste cell or are transfected into the taste cell.

Additionally, as discussed above, the claims recite that a taste cell expresses a G-protein alpha subunit polypeptide comprising greater than 70% amino acid sequence identity to a polypeptide having a sequence of SEQ ID NO: 2 and that the G-protein alpha subunit polypeptide comprises any amino acid sequence of SEQ ID NO: 2 (see for example, claims 1 and 8). However, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins,

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this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, *Genome Research* 10:398-400; Skolnick et al., 2000, *Trends in Biotech.* 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, *Trends in Genetics* 14:248-250; Smith et al., 1997, *Nature Biotechnology* 15:1222-1223; Brenner, 1999, *Trends in Genetics* 15:132-133; Bork et al., 1996, *Trends in Genetics* 12:425-427).

Due to the large quantity of experimentation necessary to identify a class of compounds to put into contact with a taste cell, to generate the infinite number of polypeptide derivatives recited in the claims and possibly screen same for activity, and to modulate signal transduction in taste cells with numerous G-protein alpha subunit polypeptide variants and any taste cell specific G protein coupled receptor, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide G-protein alpha subunit polypeptide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any specific taste cell specific G protein coupled receptors or structural or functional limitations,

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undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

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Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

* Wilkie et al. Proc Natl Acad Sci USA 88 : 10049-10053, 1991. (Wilkie et al. teaches SEQ ID NO : 2 of the instant application.)

Takami et al. Molec Brain Res 22 : 193-203, 1994.

Margolskee. U.S. Patent 6,008,000

Zuker et al. U.S. Patent 6,383,778

Adler et al. Cell 100 : 693-702, 2000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148.

The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

BEB *BEB*
Art Unit 1647
February 4, 2003

Elizabeth C. Kemmner

ELIZABETH KEMMNER
PRIMARY EXAMINER